ANALYSIS

25(107), January, 2021

ISSN 2321–7359 EISSN 2321–7367

Medical Science

The immediate effect of hemodialysis on thyroid function

Hanin A Alamoudi[1], **Reem M Alzahrani**[1], **Asya A Hawsa**[1], **Sara O Lary**[1], **Alaa M Awlia**[1], **Haneen H Alothmani**[1], **Nada A Zaher**[1], **Rana H Mosli**[2], **Hanadi M Alhozali**[3], **Hala H Mosli**[3], **Mazin A Merdad**[4]

[1]Faculty of Medicine, King Abdul-Aziz University, Jeddah, Saudi Arabia
[2]Clinical Nutrition Department, Faculty of Applied Medical Sciences, King Abdul-Aziz University, Jeddah, Saudi Arabia
[3]Department of Internal Medicine, King Abdul-Aziz University, Jeddah, Saudi Arabia
[4]Department of Otolaryngology-Head and Neck Surgery, King Abdul-Aziz University, Jeddah, Saudi Arabia

Citation

Hanin A Alamoudi, Reem M Alzahrani, Asya A Hawsa, Sara O Lary, Alaa M Awlia, Haneen H Alothmani, Nada A Zaher, Rana H Mosli, Hanadi M Alhozali, Hala H Mosli, Mazin A Merdad. The immediate effect of hemodialysis on thyroid function. *Medical Science*, 2021, 25(107), 112-119

ABSTRACT

The prevalence of chronic kidney disease (CKD) is rapidly increasing globally. There has been an established association between CKD and thyroid dysfunction. Hemodialysis appears to alter thyroid hormone levels. The purpose of this research was to determine the immediate impact of hemodialysis sessions on thyroid hormone levels. This prospective research was conducted in the Hemodialysis Unit at King Abdul-Aziz University Hospital (KAUH), Jeddah, Saudi Arabia. We reviewed 40 consecutive patients undergoing hemodialysis from November 2018 to January 2019, excluding those aged ≤ 18 years, cancer patients, and pregnant women. We analyzed thyroid-stimulating hormone (TSH), free triiodothyronine (T3), and free thyroxine (T4) levels before and after a single hemodialysis session, considering the presence of any previous thyroid dysfunction. The study population was divided according to their thyroid function markers into low, normal, and high levels. Of the study patients, 27.5% and 30% had low free T3 levels pre-dialysis and post-dialysis, respectively. Low free T4 levels were observed in 27.5% of pre-dialysis patients compared to 25% of post-dialysis patients. High TSH levels were found in 15% of pre-dialysis patients and 17.5% of post-dialysis patients. The mean free T3 and free T4 levels were significantly higher post-dialysis ($p \leq 0.01$). Longer dialysis duration was significantly associated with higher TSH levels post-dialysis. In conclusion, thyroid function markers were disturbed after a single dialysis session. Longer dialysis duration was associated with changes in TSH levels, supporting the development of hypothyroidism.

Keywords: Thyroid, hemodialysis, thyroid-stimulating hormone, triiodothyronine, thyroxine

1. INTRODUCTION

Chronic kidney disease (CKD) is a worldwide epidemic of 11-13 percent of the world's population with a rapidly increasing incidence (Hill et al., 2016). The occurrence of CKD in the general community is indeed unconfirmed in the Middle Eastern countries.

Nevertheless, the frequency of end-stage renal disorder (ESRD) per million population (PMP) is predicted to have been 100-140 cases per year (Shaheen and Souqiyyeh, 2010), with almost 76% of the patients being on regular hemodialysis (Shaheen et al., 2020). CKD is defined as a glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2 for at least 3 months, while ESRD is defined as a GFR of less than 15 mL/min/1.73 m^2—the stage requiring dialysis or transplant (Malekmakan et al., 2018). Regionally in Saudi Arabia, the Saudi Center of Organ Transplantation (SCOT) reported in 2017 that the prevalence of ESRD treated by dialysis is estimated to be 604 cases PMP, while the incidence is estimated at 163 cases PMP per year. In addition to a 12% increase in the net annual dialysis population, nearly 93% of the dialysis patients are treated by hemodialysis. The net yearly growth is attributed to two main reasons: diabetic nephropathy and hypertensive nephropathy, with a percentage increase of 39 and 36.5, respectively (Annual Report for Organ Transplantation in Kingdom of Saudi Arabia. 2017).

Many functional interactions are observed between the kidneys and the thyroid gland (Basu, 2012). Thyroid hormones have a crucial role in kidney development, and any alteration in the thyroid status can affect renal function. Conversely, the kidney influences the thyroid physiology, and changes in thyroid hormone levels are seen in patients receiving renal therapy, both in the form of renal transplantation or dialysis (Iglesias et al., 2017). Patients with CKD, even those undergoing hemodialysis have a higher incidence of thyroid problems than the wider public (Lo et al., 2005; Rhee et al., 2016). This is believed to be due to alterations in thyroid hormone synthesis, metabolism, and regulation (Lo et al., 2005; Rhee et al., 2015). The most-reported thyroid abnormalities among these patients are hypothyroidism and subclinical hypothyroidism, with increased mortality associated with hypothyroidism (Lo et al., 2005; Chonchol et al., 2008; Rhee et al., 2015; Fan et al., 2016).

Previous studies determining whether long-term hemodialysis impacts the alteration of thyroid functions among CKD patients undergoing hemodialysis are limited (Chonchol et al., 2008; Lo et al., 2017), and the immediate effect of hemodialysis on thyroid functions has not been fully explored. This study aimed to evaluate the thyroid status among hemodialysis patients and detect any immediate significant alterations in thyroid function after the dialysis sessions.

2. METHODOLOGY

Study design and setting

A prospective study including 40 consecutive patients was conducted from November 2018 to January 2019 in the Hemodialysis Unit at KAUH, Jeddah, Saudi Arabia.

Ethical approval

The Institutional Review Board approved this study at King Abdul-Aziz University. Signed informed consent was received from all the patients before their enrollment in the study. The ethical approval reference number 356-18.

Study participants

Forty patients undergoing hemodialysis for CKD at King Abdul-Aziz University Hospital were included, and data regarding their age, gender, nationality, body mass index (BMI), and the primary cause of renal failure were collected, either from the patients' charts or from the hospital's electronic records system.

The thyroid-stimulating hormone (TSH), free triiodothyronine (T3), and free thyroxine (T4) levels were analyzed before and after a single hemodialysis session, as well as whether the patients had any previously diagnosed thyroid dysfunction and whether they were on any thyroid medications. Additional data, including the patients' pre-existing co-morbidities and previous exposure to contrast dyes, were also collected.

Inclusion and exclusion criteria

All patients undergoing hemodialysis, aged 18–80 years, with pre-existing thyroid functional abnormalities were included in this research. Participants aged under 18 years, cancer sufferers, and pregnant women were excluded.

Statistical analysis

The analysis was performed utilizing IBM SPSS Statistics 25 (Armonk, NY, USA). Descriptive statistics were done to analyze sample characteristics, means and standard deviations were calculated for continuous variables and counts, and percentages were calculated for categorical variables. For thyroid function parameters, only TSH was log-transformed as it was not normally distributed. The distribution of patients in each T3, T4, and TSH category (low, normal, and high) was estimated. Paired t-test was used to compare thyroid function parameters pre-and post-dialysis. To examine the associations between thyroid function parameters and patient characteristics, the mean change of each parameter (T3, T4, and TSH) pre-and post-dialysis was calculated.

T-test were used to compare the mean change across patient categories (e.g., gender [male vs. female], nationality [Saudi vs. non-Saudi], duration of dialysis [> 9 years vs. ≤ 9 years], and so forth).

Pearson correlation was used to examine the correlation between post-dialysis thyroid function parameters and duration of dialysis (in years). To further evaluate the association between the duration of dialysis and thyroid function, the duration of dialysis into > 6 years vs. ≤ 6 years and > 9 years vs. ≤ 9 years was categorized. The association between duration of dialysis categories and indicators of hypothyroidism (low T3, low T4, and high TSH) using Fisher's exact test was examined. A significance level of 0.05 was applied in this study.

3. RESULTS

Clinical characteristics of the study population

This study was conducted on 40 consecutive patients undergoing hemodialysis at the Hemodialysis Unit at KAUH, who met the inclusion criteria. Among them, twenty-two (55%) were females, and eighteen were males (45%). The mean age was 48 ± 18.3 years. Eight patients (20%) had an underlying thyroid disorder, 29 (72.5%) patients had no underlying thyroid disorder, and 3 (7.5%) of them were not known. The mean duration of dialysis was 6.96 ± 5.41 years. The mean BMI was 23.1 ± 6.18 (Kg/m^2). Most of the cases, 29 (72.5) received Heparin as an anticoagulant, and in the rest (11, 27.5%) received Enoxaparin. Eighteen (45%) patients were previously exposed to contrast, 14 (35%) did not expose to contrast, and 8 (20%) did not know (Table 1).

Table 1 The study population clinical characteristics.

Variable	Value
Age (Year)	48.0 ± 18.3
Sex	
Male	18 (45 %)
Female	22 (55%)
History of thyroid disorder	
Yes	8 (20)
No	30 (75)
Unknown	2 (5)
Duration of dialysis (Year)	6.96 ± 5.41
Body mass index (BMI) (Kg/m^2)	23.1 ± 6.18
Administration of anticoagulants	
Heparin	29 (72.5)
Enoxaparin	11 (27.5)
Previous exposure to contrast	
Yes	18 (45)
No	14 (35)
Unknown	8 (20)

Data are presented as number and % or as mean ± SD (n = 40).

Distributions of the thyroid function parameters pre- and post-hemodialysis among CKD patients

Thyroid function markers were assessed before and after hemodialysis and were divided into low, normal, and high levels. Normal level of free T3 was found in 29 (72.5%) pre-dialysis patients versus 28 (70%) in post-dialysis patients.

Table 2 Distribution of the thyroid function parameters pre- and post-hemodialysis among CKD patients.

Parameters	Pre-Dialysis			Post-Dialysis		
	Low	Normal	High	Low	Normal	High
Free T3	11 (27.5)	29 (72.5)	-	12 (30.0)	28 (70.0)	-
Free T4	11 (27.5)	28 (70.0)	1 (2.50)	10 (25.0)	30 (75.0)	-
TSH	-	34 (85)	6 (15)	-	33 (82.5)	7 (17.5)

Data are presented as number and (% of cases) (n=40).

CKD: Chronic kidney disease; T3: Triiodothyronine; T4: Thyroxine; TSH: Thyroid-stimulating hormone.

Free T4 was present in 28 (70%) pre-dialysis patients versus 30 (75%) in post-dialysis patients. 34 (85%) pre-dialysis patients had normal TSH levels versus 33 (82.5) patients in the post-dialysis group. Eleven patients (27.5%) had low free T3 pre-dialysis compared to 12 patients (30%) post-dialysis. No patient had a high level of the free T3 hormone. Free T4 low levels were noted in also 11 patients (27.5%) pre-dialysis compared to 10 patients (25%) post-dialysis. However, one patient (2.5%) had high levels of Free T4. High TSH levels were found in 6 patients (15%) pre-dialysis and 7 patients (17.5%) post-dialysis (Table 2).

Serum thyroid function markers pre- and post-hemodialysis among CKD patients

The mean free T3 level post-dialysis was significantly higher than pre-dialysis, the free T3 level ($p = 0.01$). Additionally, the mean free T4 level post-dialysis was significantly higher in comparison with the mean free T4 level pre-dialysis ($p < 0.01$). There was no significant difference between the mean TSH of the pre-dialysis and the post-dialysis ($p = 0.06$) (Figure 1).

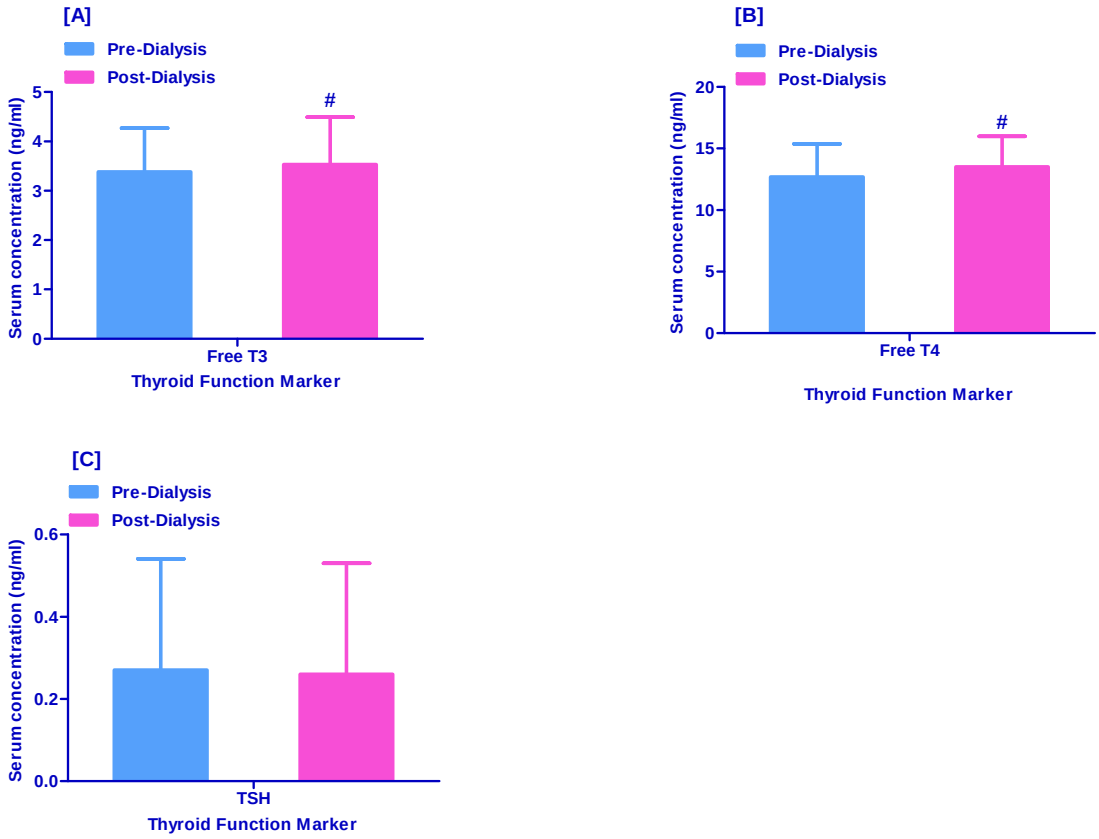

Figure 1 Thyroid function markers pre- and post-hemodialysis among CKD patients. [A] Free T3, [B] Free T4, and [C] TSH
Data are presented as mean ± SD (n = 40). # Significantly difference compare to the pre-dialysis group ($p \leq 0.01$). CKD: Chronic kidney disease. T3: Triiodothyronine; T4: Free Thyroxine; TSH: Thyroid-stimulating hormone.

Associations between mean changes in thyroid function markers and patient characteristics

Regarding the association between the mean change in thyroid function parameters and patients' characteristics, it was observed that female sex was significantly associated with mean difference of TSH level ($p = 0.04$), along with those who had been on dialysis for more than nine years ($p < 0.01$). However, we did not find a significant association between mean differences of free T3 and free T4 with the duration of dialysis. Furthermore, pre-dialysis administration of Heparin and previous exposure to contrast were both significantly associated with the mean difference of free T3 ($p < 0.01$ and $p = 0.03$, respectively) (Table 3).

Table 3 Associations between mean change in thyroid function markers and patient characteristics

Characteristics	Mean change in free T3	p-value	Mean change in free T4	p-value	Mean change in TSH	p-value
Sex						
Male	0.07 ± 0.37	0.24	0.58 ± 0.64	0.24	-0.04 ± 0.05	0.04
Female	0.21 ± 0.35		0.97 ± 1.39		-0.0004 ± 0.05	
Nationality						
Saudi	0.16 ± 0.28	0.84	0.94 ± 1.12	0.75	-0.02 ± 0.04	0.66
Non-Saudi	-0.06 ± 0.44		0.79 ± 2.61		-0.01 ± 0.06	
History of thyroid disorder						
Yes	-0.05 ± 0.61	0.16	0.48 ± 1.32	0.31	-0.04 ± 0.05	0.19
No	0.19 ± 0.28		0.98 ± 1.04		-0.01 ± 0.05	
Duration of dialysis (Year)						
> 9 Years	0.24 ± 0.41	0.38	1.05 ± 1.12	0.78	0.02 ± 0.03	0.009
≤ 9 Years	0.12 ± 0.35		0.71 ± 1.13		-0.03 ± 0.05	
Administration of Heparin						
Yes	0.24 ± 0.33	0.006	0.93 ± 1.14	0.23	-0.007 ± 0.05	0.07
No	-0.10 ± 0.34		0.44 ± 1.04		-0.04 ± 0.06	
Previous exposure to contrast						
Yes	0.28 ± 0.35	0.03	1.09 ± 1.28	0.14	-0.02 ± 0.05	0.97
No	0.04 ± 0.34		0.56 ± 0.95		-0.02 ± 0.06	

Data are presented as mean ± SD (n=40)

T3: Triiodothyronine; T4: Thyroxine; TSH: Thyroid-stimulating hormone.

Differences between groups were examined using an independent sample t-test.

Associations between duration of dialysis and markers of hypothyroidism

Results showed that a significant, positive correlation ($r = 0.45$, $p < 0.001$) between the post-dialysis TSH concentration and the duration of the dialysis was found. There was no significant correlation between free T3 and free T4 with the duration dialysis ($r = -0.02$, $p = 0.88$ and $r = -0.16$, $p = 0.32$, respectively). Regarding the duration of dialysis and markers of thyroid function, we observed that longer duration on dialysis was significantly associated with higher TSH levels post-dialysis. Patients who had been on dialysis for more than six years had a p-value of 0.04, and those on dialysis for more than nine years had a p-value of <0.001 (Table 4).

Table 4 Associations between duration of dialysis and markers of hypothyroidism

Characteristics	Low Free T3 Post-Dialysis (n=12)	p-value	Low Free T4 Post-Dialysis (n=10)	p-value	High TSH Post-Dialysis (n=7)	p-value
Duration of dialysis (Year)						
> 6 Years	7 (58.3)	0.49	6 (60)	0.47	6 (85.7)	0.04
≤ 6 Years	5 (41.7)		4 (40)		1 (14.3)	
Duration of dialysis (Year)						
> 9 Years	4 (33.4)	0.45	4 (40)	0.23	6 (85.7)	0.000
≤ 9 Years	8 (66.7)		6 (60)		1 (14.3)	

Data are presented as number and % (n=40).

T3: Triiodothyronine; T4: Thyroxine; TSH: Thyroid-stimulating hormone.

Differences between groups were examined using Fisher's exact test.

4. DISCUSSION

Since the kidneys are intricately involved in the hormonal physiology within the human body, it is not unexpected for the thyroid physiology to be disturbed and affected by impaired kidney function. Therefore, this study was conducted to assess the thyroid functional status among hemodialysis patients and ascertain the immediate impact of dialysis on the thyroid function parameters. In 1988, Kaptein et al. reported that 65.5% of euthyroid patients with ESRD had low levels of FT3. Similarly, there was a significantly higher incidence of reduced FT4 levels, by 12.9%, among these patients (Kaptein et al., 1988). A previous study demonstrated that almost 46% of ESRD patients had reduced FT3 concentrations, indicating that the prevalence of low FT3 levels was extraordinarily high and predominantly found in ESRD patients (Singh et al., 2016). In accordance with that, Song et al. registered a corresponding increase in the distribution of reduced T3 levels with the progression of CKD stages (Song et al., 2008). Furthermore, patients with ESRD and elevated serum-free T3 had quite a lesser probability of mortality than individuals with low serum-free T3 (Zoccali et al., 2006). Both these observations contribute to the hypothesis that thyroid dysfunction is more prevalent in ESRD patients and that the presence of thyroid dysfunction in this cohort might be a prognosticator, proffering a high risk to this group of patients, as it is found that low FT3 is an independent mortality predictor in hemodialysis patients (Zoccali et al., 2006).

Our findings are in line with previous literature that observed a significantly higher FT3 and FT4 concentrations immediately following hemodialysis sessions (van Leusen and Meinders, 1982; Sakurai et al., 1988; Alsaran et al., 2011). Similarly, Alsaran et al. found that the levels of both FT3 and FT4 increased significantly post dialysis, although no change in the TSH levels was observed (Alsaran et al., 2011). In 1973, Silverberg et al. believed that the post-dialysis increases in mean FT4 fraction and the mean FT4 might be attributed to heparin Heparin's inhibitory effect on the binding site of thyroxine that helps it attach onto its carrying proteins (Silverberg et al., 1973). Like these findings, other studies have found a transient increase in T4 levels following hemodialysis (Basu, 2012; Mohamedali et al., 2014). Laji et al. described the changes in serum FT3 and FT4 after heparinization in 4 patients, and they found that FT3 and FT4 levels increased during heparin treatment (Laji et al., 2001). Antithetical to these studies, our results indicated that heparin administration was only associated with FT3.

In a trial conducted in 2017, Joan et al. have found that repeated hemodialysis has no major long-term impact on thyroid function (Lo et al., 2017). In contrast to this finding, we observed a significant association between TSH levels and hemodialysis duration of more than nine years. However, the post-dialysis TSH levels positively correlated to dialysis duration. Therefore, more dialysis sessions lead to increased disturbance of TSH levels.

This study has some limitations. Owing to the size of our dialysis unit, our sample size was relatively small. Another limitation we faced was the lack of funding; this prevented us from testing the pre- and post-dialysis changes in thyroid hormones over a more extended period on a more frequent basis.

5. CONCLUSION

Immediate changes in thyroid markers were observed after a single dialysis session. Patients who had been on dialysis for more prolonged periods had changes in TSH levels, which support our hypothesis that CKD patients on dialysis are susceptible to thyroid dysfunction, mainly developing hypothyroidism.

Acknowledgments

We would like to thank the nursing staff working at the dialysis unit and the lab technicians at KAUH for their valuable efforts in helping us with data collection.

Funding

No funding to declare.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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Peer-review

External peer-review was done through double-blind method.

Article History

Received: 09 December 2020

Reviewed & Revised: 09/December/2020 *to* 11/January/2021

Accepted: 11 January 2021

E-publication: 15 January 2021

ANALYSIS ARTICLE

P-Publication: January 2021

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